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#4	Search (pharmaceutical) AND ("GPR65" [TIAB] OR "GPR-65" [TIAB] OR "GPR 65" [TIAB] OR "G-protein coupled receptor 65" [TIAB] OR "hTDAG8" [TIAB] OR "hTDAG-8" [TIAB] OR "hTDAG 8" [TIAB] OR "Psychosine receptor" [TIAB] OR "T cell-death associated protein 8" [TIAB] OR "TDAG8" [TIAB] OR "TDAG-8" [TIAB] OR "TDAG 8" [TIAB])	18:56:10	<u>0</u>
#3	Search (camp) AND ("GPR65" [TIAB] OR "GPR-65" [TIAB] OR "GPR 65" [TIAB] OR "G-protein coupled receptor 65" [TIAB] OR "hTDAG8" [TIAB] OR "hTDAG-8" [TIAB] OR "hTDAG 8" [TIAB] OR "Psychosine receptor" [TIAB] OR "T cell-death associated protein 8" [TIAB] OR "TDAG8" [TIAB] OR "TDAG-8" [TIAB] OR "TDAG 8" [TIAB])	18:55:50	<u>3</u>
#2	Search (disorder) AND ("GPR65" [TIAB] OR "GPR-65" [TIAB] OR "GPR 65" [TIAB] OR "G-protein coupled receptor 65" [TIAB] OR "hTDAG8" [TIAB] OR "hTDAG-8" [TIAB] OR "hTDAG 8" [TIAB] OR "Psychosine receptor" [TIAB] OR "T cell-death associated protein 8" [TIAB] OR "TDAG8" [TIAB] OR "TDAG-8" [TIAB] OR "TDAG 8" [TIAB])	18:55:40	<u>0</u>
#1	Search (disease) AND ("GPR65" [TIAB] OR "GPR-65" [TIAB] OR "GPR 65" [TIAB] OR "G-protein coupled receptor 65" [TIAB] OR "hTDAG8" [TIAB] OR "hTDAG-8" [TIAB] OR "hTDAG 8" [TIAB] OR "Psychosine receptor" [TIAB] OR "T cell-death associated protein 8" [TIAB] OR "TDAG8" [TIAB] OR "TDAG-8" [TIAB] OR "TDAG 8" [TIAB])	18:55:23	<u>0</u>

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Symbol	Name	Synonyms	Or...
 GPR65	G protein-coupled receptor 65	G-protein coupled receptor 65, hTDAG8, Psychosine receptor, T cell-death associated protein 8, TDAG8	Ho...
UniProt	Q8IYL9, O75819		
OMIM	604620		
NCBI Gene	8477	more than 1,500 organisms. 80,000 genes. 12 million sentences.	
NCBI RefSeq	NP_003599	...always up-to-date	
NCBI RefSeq	NM_003608		
NCBI UniGene	8477		
NCBI Accession	BC035633, BC071715		

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2. Furthermore, RhoA activation and actin rearrangement were elicited by acid-stimulated TDAG8★. [2005]

G protein [?] -coupled receptors GPR4★ and TDAG8★ are oncogenic and overexpressed in human cancers. [2005]

The subfamily of G protein-coupled receptors comprising GPR4★, OGR1★, TDAG8★, and G2A★ was originally characterized as a group of proteins mediating biological responses to the lipid messengers sphingosylphosphorylcholine (SPC), lysophosphatidylcholine (LPC), and psychosine. [2006]

Here we show that GPR4★ also malignantly transforms NIH3T3 cells and that TDAG8★ malignantly transforms normal mammary epithelial cell line NMuMG. [2004]

G2A★, T cell death-associated gene 8 (TDAG8 [?]★), ovarian cancer G protein-coupled receptor 1★ (OGFR) G protein-coupled receptor 4 [?]★ (GPR4★) form a group of structurally related G protein-coupled receptors (originally proposed to bind proinflammatory lipids. [2005])

Receptors of the endothelial differentiation gene family are activated by S1P [?] (S1P(1-5)) or LPA (LPA(1-3)); two distantly related receptors are activated by LPA (LPA(4/5)); the GPR(3/6/12) receptors have a high constitutive activity and are further activated by S1P [?] and/or SPC; and receptors of the OGR1★ cluster (OGR1★, GPR4★, G2A★, 1) appear to be activated by SPC, LPC, psychosine and/or protons. [2007]

Identification of T cell death-associated gene 8 (TDAG8★) as a novel acid sensing G-protein-coupled receptor. [2005]

The gene, human TDAG8 (hTDAG8★), which belongs to the G protein [?] -coupled receptor superfamily, encode a protein of 337 amino acids. [1998]

We conclude that members of this GPCR [?] group exhibit differential sensitivity to extracellular protons, and that expression of TDAG8 [?]★ by immune cells may regulate responses in acidic microenvironments. [2005]

In particular, dexamethasone caused down-regulation of genes promoting DP thymocyte survival (e.g., Notch1 suppressor of cytokine signaling 1, and inhibitor of DNA binding 3) or modulation of genes activating cell death through the ceramide pathway (UDP-glucose ceramide glucosyltransferase, sphingosine 1-phosphate phosphatase, dihydroceramide desaturase, isoform 1, and G protein-coupled receptor 65) or through the mitochondrial machinery. [2006]

Please cite the use of iHOP as "Hoffmann, R., Valencia, A. A gene network for navigating the literature. Nature Genetics 36, 664 (2004)" and as <http://www.ihop-net.org/>".

Special thanks to Chris Sander for his continuing support.

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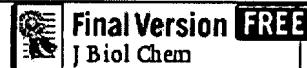
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1: [J Biol Chem. 2004 Dec 17;279\(51\):52850-9. Epub 2004 Oct 12.](#)



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Normal immune development and glucocorticoid-induced thymocyte apoptosis in mice deficient for the T-cell death-associated gene 8 receptor. [Mol Cell Biol. 2006]

Critical function of T cell death-associated gene 8 in glucocorticoid-induced thymocyte apoptosis. [J Biol Chem. 2003]

Thioredoxin-interacting protein (txnip) is a glucocorticoid-regulated primary response gene involved in mediating glucocorticoid-induced apoptosis. [Oncogene. 2006]

TDAG8 is a proton-sensing and psychosine-sensitive G-protein-coupled receptor. [J Biol Chem. 2004]

The pro-apoptotic protein Bim is a convergence point for cAMP/protein kinase A- and glucocorticoid-promoted apoptosis of lymphoid cells. [J Biol Chem. 2004]

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The glucocorticoid-induced gene tdag8 encodes a pro-apoptotic G protein-coupled receptor whose activation promotes glucocorticoid-induced apoptosis.

Malone MH, Wang Z, Distelhorst CW.

Department of Medicine, Comprehensive Cancer Center, Case Western Reserve University School of Medicine, 10900 Euclid Ave., Cleveland, OH 44106, USA.

The apoptotic action of glucocorticoids on lymphocytes makes them effective therapeutics for many lymphoid malignancies. Although it is clear that glucocorticoid-induced apoptosis requires transcription, the gene products that induce apoptosis remain unknown. Using gene expression profiles of lymphoma cell lines and primary thymocytes treated with the synthetic glucocorticoid dexamethasone, we discovered that induction of *tdag8* (T-cell death-associated gene 8) was a common event in each model system investigated. Activation of TDAG8 by its agonist psychosine markedly enhanced dexamethasone-induced apoptosis in a TDAG8-dependent manner. Expression of a TDAG8-GFP fusion protein was sufficient to induce apoptosis, and repression of endogenous TDAG8 using RNA interference partially inhibited dexamethasone-induced apoptosis. Together, these data suggest that TDAG8 is a regulator of glucocorticoid-induced apoptosis and that agonists of TDAG8 may be promising agents to improve the efficacy of glucocorticoids for the treatment of leukemia and lymphoma.

PMID: 15485889 [PubMed - indexed for MEDLINE]

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1: [Fukunaga S, Setoguchi S, Hirasawa A, Tsujimoto G.](#) Related Articles, Links

Monitoring ligand-mediated internalization of G protein-coupled receptor as a novel pharmacological approach.

Life Sci. 2006 Dec 3;80(1):17-23. Epub 2006 Aug 25.
PMID: 16978657 [PubMed - indexed for MEDLINE]

2: [Malone MH, Wang Z, Distelhorst CW.](#) Related Articles, Links

The glucocorticoid-induced gene ttag8 encodes a pro-apoptotic G protein-coupled receptor whose activation promotes glucocorticoid-induced apoptosis.

J Biol Chem. 2004 Dec 17;279(51):52850-9. Epub 2004 Oct 12.
PMID: 15485889 [PubMed - indexed for MEDLINE]

3: [Murakami N, Yokomizo T, Okuno T, Shimizu T.](#) Related Articles, Links

G2A is a proton-sensing G-protein-coupled receptor antagonized by lysophosphatidylcholine.

J Biol Chem. 2004 Oct 8;279(41):42484-91. Epub 2004 Jul 27.
PMID: 15280385 [PubMed - indexed for MEDLINE]

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